UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,889	01/25/2002	Thomas C. Hart	WFU.99-35	8219

110 7590 01/26/2004

DANN, DORFMAN, HERRELL & SKILLMAN
1601 MARKET STREET
SUITE 2400
PHILADELPHIA, PA 19103-2307

EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,889	HART, THOMAS C.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on th cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *3-6,8-12,26-29,31-33,39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7,13-25,30 and 34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Election/Restrictions

1. Applicant's election with traverse of Group I, and the mutation G1286A in the response of October 15, 2003 is acknowledged. The traversal is on the ground(s) that all claims share the special technical feature of an altered CTSC protein and thereby should be examined together. Applicants further argue that each of the variants of the CTSC share a common feature because they are all related to palmoplantar ectodetermal disorders/dysplasia and thereby all 19 variants should be examined together. It is also stated that during the PCT stage, the claims were found to have unity of invention. These arguments are not found persuasive because under PCT Rules 37 CFR 1.475 Applicants are entitled ONLY to the first product, method of making a product and method of using a product. Groups II and III are drawn to additional products (namely, proteins and antibodies) and thereby restriction is proper. Secondly, the products do not share a common structural feature since the products of group I are drawn to nucleic acids whose special technical feature is determined by the nucleotide monomers that comprise the nucleic acid; the products of group II are drawn to proteins whose special technical feature is determined by its amino acid composition and specific 3-dimensional structure; and the products of group III are drawn to antibodies whose special technical feature is determined by its amino acid composition and specific 3-dimensional structure, which are distinct from that of the proteins of group II. Further, the variants of CTSC do not share a common structural feature because each of these variants differ in their nucleotide or amino acid sequence and this variation imparts a unique functional attribute to each nucleic acid and protein. For example, a

nucleic acid having a 199-222 deletion is structurally and functionally distinct from a nucleic acid having a 445 to 446 ATGT insertion. Finally, it is noted that unity of invention at the PCT stage is not controlling over the LOU requirement at the 371 Stage of prosecution since unity of invention may be evaluated at each stage of (chapter I, chapter II, and the National stage). See MPEP 1893. 03.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, the elected invention of nucleic acids encoding a protein having a G1286A mutation and methods of detecting said nucleic acids, which encompasses Claims 1, 2, 7, 13-25, 30, 34-36, 37 and 38, has been examined herein.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2 and 7 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Because the claims do not recite a purity or size limitation, the claims read on the complete chromosome of containing the CTSC gene and the naturally occurring CTSC gene variant having a G to A substitution at position 1286. Chromosomes are products of nature and are not patentable. To overcome this rejection it is suggested that the claims be amended to include purity limitations which would distinguish the claimed compounds, as enabled by the specification, over the naturally occurring compounds. For example, this rejection may be overcome by amendment of the claims to include the terminology "isolated and

purified" and/or to provide a description of what the claimed products are "free of" relative to that of the natural source.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-25, 30 and 34-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for detecting a substitution of a G to an A at nucleotide position 1286 of the CTSC gene of SEQ ID NO: 1, methods for detecting the presence of a germline mutation at position 1286 of the CTSC gene of SEQ ID NO: 1 wherein said methods comprise screening a gamete cell for the presence of a G to an A substitution at position 1286 of the CTSC gene, does not reasonably provide enablement for methods for detecting a germline alteration in a CTSC gene wherein said methods comprise analyzing a sequence of a CTSC gene, cDNA or mRNA from any human sample for the presence of an alteration set forth in Table 1 or methods which detect any germline alteration wherein the methods comprise comparing a sequence of a CTSC DNA or RNA from a human sample with an isolated wild-type CTSC sequence provided in SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the

nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Claims 13-25 and 30 are drawn broadly to methods for detecting a germline alteration in a CTSC gene wherein said methods comprise analyzing a sequence of a CTSC gene, cDNA or mRNA from any human sample for the presence of an alteration set forth in Table 1. Claims 34-36 are drawn to methods which detect any germline alteration in a CTSC-encoding nucleic acid wherein the methods comprise comparing a sequence of a CTSC DNA or RNA from a human sample with an isolated wild-type CTSC sequence provided in SEQ ID NO: 1.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to

constitute adequate enablement". In the instant case, the specification does not enable the invention as it is broadly claimed for the following reasons:

The claims require the detection of a germline alteration in a CTSC encoding nucleic acid. The methods involve analyzing any human sample for the presence of such a mutation and/or comparing a CTSC nucleic acid to a wild-type CTSC nucleic acid. The specification teaches that familial studies were performed to detect the presence of CTSC mutations in PLS affected patients. The specification (e.g., Table 1) teaches 21 CTSC mutations found in the PLS affected patients. As stated in the specification (page 37), "(a)ll PLS affected individuals examined were homozygous for cathepsin C mutations from a common ancestor." The specification (e.g., page 18) also teaches that CTSC mutations may be associated with predisposition to keratodermal disorders and dysplasia. However, while spontaneous mutations occur relatively infrequently, such mutations do in fact occur in somatic cells and particularly in somatic cells associated with dysplasia. Accordingly, methods which analyze any human sample (as opposed to analyzing a germ cell) for the presence of an alteration in CTSC genomic DNA or RNA will detect both germline and somatic mutations. The claims do not include any of the essential steps that would allow the skilled artisan to distinguish between germline mutations and somatic mutations.

Secondly, claims 34-36 are drawn to research methods for detecting any germline alteration in a CTSC gene by comparing a sample CTSC nucleic acid to a portion of CTSC nucleic acid provided in SEQ ID NO: 1. The specification teaches that the detection of CTSC mutations is beneficial for screening and diagnosing "certain

palmoplantar keratoldermas and periodontal disease states in affected individuals" (see page 5). The identified mutations are also to be used for the development of therapeutics. The specification teaches 16 different mutations that were each identified in 1 family having a member affected with PLS or HMS; 4 different mutations that were identified in 2 families having a member affected with PLS; and 1 mutation that was identified in 3 families each having a member affected with PLS. In particular, the specification teaches a CTSC nucleic acid in which a G has been substituted with an A at nucleotide position 1286. This alteration results in the introduction of stop codon in place of a codon for tryptophan at amino acid position 429, leading to a truncated protein of 428 amino acids as compared to the wild-type CTSC protein of 463 amino acids. While several other mutations set forth in Table 1 also involve the introduction of a stop codon or premature termination codon, many of the alterations also involve single amino acid substitutions. The specification has not established that each of these alterations is associated with the occurrence of disease in the general population. At page 5, the specification states that: "Mutations or functional polymorphisms associated with the disease states are those which give rise to altered, truncated, misfolded or otherwise non-functional CTSC polypeptides. Polymorphisms in the CTSC sequence which do not affect the nature of the encoded protein are not associated with PLS, HMS or periodontal disease." Most importantly, at page 66 of the specification, it is stated that "While the mutations described in the previous examples are associated with certain pathological conditions, it is important to note that the CTSC gene contains many polymorphisms. Many of these genetic changes are not associated with the disease

state. The genetic changes assessed by the methods of the present invention must be associated with the production of an aberrant CTSC protein. The specification goes on to state that suitable assays can be performed to distinguish between "harmless polymorphisms" and mutations that give rise to PPKs and periodontal disorders. Such assays include screening for decreased CTSC mRNA stability and decreased cathepsin C enzyme activity. However, the specification does not provide sufficient guidance to enable the skilled artisan to identify mutations in addition to the G1286A mutation that are associated with PLS. While the tools are available in the art for sequencing nucleic acids and for assaying for mRNA stability and cathepsin C enzyme activity, there is no predictable means for determining which of the large number of possible alterations in the CTSC gene would be associated with PPKs and periodontal disease. As set forth in the specification (page 58), the CTSC gene is 46 Kb in length and comprises 7 exons. Screening the CTSC gene for additional mutations and performing assays to determine if any of these mutations are in fact correlated with disease can only be accomplished through trial and error experimentation. The ability to perform a molecular assay to screen for mutations does not provide one with the results of such assays and does not place one in possession of CTSC mutations associated with PPKs or periodontal diseases . Such methods provide only a starting point for performing additional research.

In view of the lack of specific guidance provided in the specification as to the identity of additional mutations (other than the G1286A mutation) that are associated with PPKs and periodontal disease and in view of the unpredictability in the art of

identifying specific mutations associated with disease, undue experimentation would be required to practice the invention as it is broadly claimed.

4. Claims 1, 2, 7, 37 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a nucleic acid molecule encoding an altered CTSC protein, said nucleic acid having at least one of the alterations set forth in table 1. The claim does not set forth any particular structure for the claimed nucleic acid but rather claims the nucleic acid broadly so as to include nucleic acids encoding any modified form of a CTSC protein, including proteins that have any amino acid substitution, deletion or addition. The claims do not define the activity of the "altered CTSC protein" and thereby include proteins having an increased or decreased or modified CTSC enzymatic activity. However, the specification teaches the wild-type CTSC nucleic acid of SEQ ID NO: 1 and teaches variants of SEQ ID NO: 1 which differ from SEQ ID NO: 1 with respect to the mutations set forth in Table 1. While isolated CTSC nucleic acids consisting of the sequence of SEQ ID NO: 1 and which differ with respect to SEQ ID NO: 1 in that the include one of the mutations set forth in Table 1 (e.g., isolated CTSC nucleic acids which comprise SEQ ID NO: 1 with the exception that said nucleic acid has an A in place of a G at nucleotide position 1286) meet the written description requirements of 35 U.S.C. 112, first paragraph, the specification does not disclose and fully characterize the claimed genus of any nucleic acid encoding an altered CTSC having at least one of

the alterations set forth in Table 1. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, 21 members of the genus of CTSC nucleic acids have been identified. However, the claims as written are inclusive of a huge genus of CTSC nucleic acids which differ from SEQ ID NO: 1 and which differ from the CTSC nucleic acids set forth in Table 1 at any position in the CTSC gene, including the promoter, 3' and 5' untranslated regions, exon and intron

regions of the CTSC gene. While one could contemplate a nucleotide substitution at each and every position in the CTSC gene, such substitutions are not considered to be equivalent to polymorphisms. Rather, alterations in the CTSC gene represent a distinct group of nucleotide variations which are expected to occur at only specific locations within the gene and consist of specific nucleotide alterations. Accordingly, knowledge of the sequence of the wild-type CTSC gene does not allow the skilled artisan to envision all of the contemplated nucleic acids encoding altered CTSC proteins encompassed by the claimed genus.

Further, with respect to claims 2, 7, 37 and 38, these claims are inclusive of probes and oligonucleotides that specifically hybridize or which are specifically hybridizable to a human altered-CTSC encoding nucleic acid, wherein the altered CTSC nucleic acids have one of the alterations set forth in Table 1. Again, the specification has not adequately described a representative number of nucleic acids encoding altered CTSC proteins which include one or more of the mutations set forth in Table 1 and include any additional unstated modification. The claims do not adequately set forth the structure of the claimed probes and oligonucleotides. Rather, the probes and oligonucleotides are defined in terms of their ability to hybridize to CTSC nucleic acids encoding altered CTSC proteins under unspecified hybridization conditions. It is noted that the specification discusses the concept of "specifically hybridizes." However, it is not clear from this discussion what would constitute a probe that specifically hybridizes to an altered CTSC-encoding nucleic acid. The specification states that such a probe need not be fully complementary to its target, but must anneal specifically under a set of

pre-determined conditions. Yet the claims do not set forth such conditions and the specification and claims do not clarify whether probes that specifically hybridize only to the altered CTSC-encoding nucleic acid or whether such probes may also cross-hybridize to a lesser degree to other nucleic acids. The claims do not set forth any structural features for the claimed probes and do not state any conditions for hybridization. Accordingly, the probes and nucleic acids are not adequately described in terms of their structural and functional properties. Therefore, Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 7, 13-25, 30, 34-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 7, 13-25, 30, 34-38 are indefinite over the recitation of "the alterations set forth in Table 1" because this phrase lacks proper antecedent basis. Claim 1 does not refer to any "alterations" per se, but rather refers to mutations. Also, the table itself does not specifically state what is considered to be the wild-type

sequence and what is considered to be the altered sequence. Additionally, it is not clear as to whether claim 1 includes nucleic acids having a G at position 1286 or includes only nucleic acids having an A at position 1286.

Claims 2 and 7 are indefinite over the recitation of "probe specifically hybridizable to a human altered CTSC-encoding nucleic acid." The ability to hybridize (i.e., "hybridizable") is a latent characteristic and the claims do not set forth the criteria for determining whether a probe specifically hybridizes or does not specifically hybridize to a target sequence. Further, the specification at pages 10-11 discusses the concept of "specifically hybridizes" but it is not clear from this discussion what would constitute a probe that specifically hybridizes to an altered CTSC-encoding nucleic acid. The specification states that such a probe need not be fully complementary to its target, but must anneal specifically under a set of pre-determined conditions. However, the claims do not set forth such conditions and the specification and claims do not clarify whether probes that specifically anneal only to the altered CTSC-encoding nucleic acid or whether such probes may also cross-hybridize to a lesser degree to other nucleic acids. The claims do not set forth any structural features for the claimed probes and do not state any conditions for hybridization and thereby one of skill in the art cannot determine the meets and bounds of the claimed invention. Similarly, claims 15, 17, 37 and 38 are also indefinite over the recitation of "specifically hybridize".

Claims 2, 7, 15, 16, 17, 18, 21, and 22 are indefinite over the recitation of "wild-type CTSC" because it is not clear as to what constitutes the wild-type sequence. The specification at page 5 states that "the wild-type CTSC nucleic acid sequence and its

encoded amino acid sequence are known. See SEQ ID NOS: 1-3 provided herein." However, the specification does not clarify that each Applicants intend to define wild-type CTSC nucleic acids as those nucleic acids consisting of the sequence of SEQ ID NO: 1 and 2. Since the art teaches different versions of the CTSC nucleic acid (see Rao et al. Journal of Biological Chemistry. 1997. 272: 10260-10265), it is not clear as to what nucleotide sequence is intended to be encompassed by "the wild-type CTSC" nucleic acid.

Claim 7 is indefinite over the recitation of "said altered CTSC DNA" because this phrase lacks proper antecedent basis. While the claim previously refers to an "altered CTSC- encoding nucleic acid" the claim does not previously refer to an "altered CTSC DNA."

Claims 13-25, and 30 are indefinite. The claims are drawn to a method for detecting a germline alteration. However, the claims recite only a single step of analyzing the sequence of a CTSC gene, RNA, or cDNA. The claims do not clarify how the step of analyzing a sequence results in the detection of a germline alteration. Accordingly, it is not clear as to whether the claims are intended to be limited to methods for detecting a germline alteration or methods for analyzing the sequence of a CTSC gene, RNA, or cDNA. Additionally, claims 15, 17 and 24 are further indefinite in that the method results in the detection of the presence of a germline alteration in the sample, but does not state that the method results in the detection of a germline alteration in the CTSC gene. Claim 19 is further indefinite in that the method results in

the detection of the presence of an allele in the sample, but does not state that the method results in the detection of a germline alteration in the CTSC gene.

Claim 25 is indefinite over the recitation of "said second fragment corresponding to said first fragment" because "corresponding" is not an art recognized term to describe the relationship between two nucleic acid sequences. It is not clear whether this refers to sequence homology/similarity or to sequence complementarity and it is not clear what percentage of homology or complementarity is encompassed by "corresponding" or under what types of conditions "corresponding" nucleotides are determined.

Claims 34-36 are indefinite. The claims are drawn to a method for detecting a germline alteration. However, the claims recite only a single step of comparing a CTSC gene, RNA, or cDNA with a wild-type CTSC nucleic acid. The claims do not clarify how the step of comparing the sequences results in the detection of a germline alteration. Accordingly, it is not clear as to whether the claims are intended to be limited to methods for detecting a germline alteration or methods for analyzing the sequence of a CTSC gene, RNA, or cDNA.

Claims 34-36 are indefinite over the recitation of "an isolated wild type CTSC sequence as provided in SEQ ID NO: 1" because it is not clear as to whether the DNA or RNA from the sample is compared to the full length sequence of SEQ ID NO: 1 or to any fragment of any length of SEQ ID NO: 1.

Claim 35 is indefinite over the recitation of "said altered CTSC mRNA" because this phrase lacks proper antecedent basis.

Claim 36 is indefinite over the recitation of "said altered CTSC encoding nucleic acid" because this phrase lacks proper antecedent basis.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Rao.

Rao (see pages 10261-10262) teaches a method which includes the steps of determining the nucleotide sequence of the CTSC gene (referred to therein as the human dipeptidyl-peptidase I gene; see page 10260) from human spleen cells and comparing this sequence to a CTSC wild-type gene obtained from the ileum. Rao teaches the 4 alterations in the spleen DNA versus the ileum DNA. It is noted that the claims as written include methods which compare a sample of nucleic acid to a wild type CTSC sequence provided in SEQ ID NO: 1. That is, the claims include a comparison of the sample DNA to nucleic acids comprising portions of SEQ ID NO: 1. Thereby, the claims encompassed by the method of Rao which compares the sample nucleic acid to a CTSC nucleic acid having sequences of SEQ ID NO: 1. Further, it is noted that the recitation in the preamble does not result in a manipulative difference in the method steps when compared to the prior art disclosure. Since the method step recited in the claim is the same as the step set forth by Rao, the method of claim 34 is anticipated by the disclosure of Rao.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers
January 21, 2004

CARLA J. MYERS
PRIMARY EXAMINER